UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,893	09/12/2003	Charles J. Link	05237.0003.CPUS01	4317

22930 7590 11/02/2006

HOWREY LLP
C/O IP DOCKETING DEPARTMENT
2941 FAIRVIEW PARK DR, SUITE 200
FALLS CHURCH, VA .22042-2924

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,893	LINK ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *9,10,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-23 and 26-28* is/are rejected.

7)☒ Claim(s) *29-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/25/2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/04, 6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 8/22/2006, in which claims 7 and 22 were amended. Currently, claims 1-32 are pending.

Election/Restrictions

Applicant's election with traverse of "SAVI" as the species of method step of determining the identity of the protein fused to the marker peptide, and "pGT-fs0" as the viral vector used in the step of introducing the polynucleotide into the genome of the host cell in the reply filed on 8/22/2006 is acknowledged. The traversal is on the ground(s) that the viral vectors of claim 22 are members of a Markush group and all vectors possess at least one property in common, which is responsible for their function in the claimed process. This is not found persuasive, because the presence of a shared property does not prohibit the election of species requirement. A Markush-type claim may be used to recite alternatives that have at least one property in common which is mainly responsible for their function in the claimed process. However, the Examiner is not required to examine all members of the Markush group unless they are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden. MPEP § 803.02. In the instant case, the each of the vectors recited in claim 22 has a distinct chemical structures and biological functions. For example, some vectors have a splice acceptor and splice donor (e.g. Figures 2h and 2i), and some vectors have a splice acceptor and a polyA cleavage site (e.g. Figure 2j, Drawings submitted 6/25/2004). Some vectors encode hrGFP (e.g. Figures 2h and 2j), and some vectors encode influenza haemaglutinin HA eptiopes (e.g. Figure 2i, Drawings submitted 6/25/2004). Claim 22 is drawn to 28 distinct

vectors, with each vector requiring a separate search of the patent and non-patent literature. Accordingly, searching all of the vectors of claim 22 would impose a serious search burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 24 and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/22/2006. Applicant indicated that claims 9 and 10 were withdrawn from consideration. Claims 24 and 25 depend from claims 9 and 10, respectively, and thus are withdrawn from consideration.

Currently, claims 1-8, 11-23 and 26-32 are under consideration.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) and 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application Nos. 09/811,842 (hereinafter the '842 application) and 60/190,678 (hereinafter the '678 application), fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The specifications of the prior-filed applications do not disclose the specific steps recited in the claimed method. The instant claims require the use of a construct comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence, ii) a complementary sequence of a first type IIS restriction enzyme recognition sequence, iii) an oligonucleotide sequence encoding an assayable marker peptide, iv) a sequence of a second type IIS restriction enzyme recognition sequence, and v) a splice donor consensus sequence. In the '842 application, the only reference to a vector that meets the structural limitations of the claims is found in Figure 2D. The specification describes this vector as a "transfection cassette" (e.g. page 9, paragraph 1). The '678 application fails to disclose any constructs that meet the structural limitations of the claims. Furthermore, the specification of the '842 application does not teach the method of SAVI where at least one type IIS restriction enzyme cleaves upstream and downstream of the peptide marker sequence. The specification of the '842 application teaches that a restriction enzyme is used which cuts at a known site within one end of the expression construct (e.g. page 59, 1st full paragraph; depicted in Figure 17). Thus prior-filed applications do not disclose the specific steps required by the claims.

Accordingly, prior-filed Application Nos. 09/811,842 and 60/190,678 do not provide adequate support under 35 USC § 112, first paragraph, for claims 1-8, 11-23 and 26-32.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or

provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/458,152 (hereinafter the '152 application), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The disclosure of the '152 application fails to provide support for the sorting of cells into monoclonal subgroups of genetically identical cells. At page 32, lines 4-9, the specification of the '152 application teaches away from isolating each individual cell, and instead teaches the sorting of cells based upon their expression of the marker gene such that cells are grouped together by virtue of demonstrating an approximately equivalent level of marker gene expression. Instant claims 3, 5 and 28 require the step of sorting cells into monoclonal subgroups of genetically identical cells. The prior-filed application does not provide adequate support for this step.

Accordingly, prior-filed Application No. 60/458,152 does not provide adequate support under 35 USC § 112, first paragraph for claims 3, 5 and 28. Claims 7, 8, 11-23, 26, 27 and 29-32 depend directly or indirectly from claims 3 or 5 and thus lack support in Application No. 60/458,152 for the same reasons as applied to claims 3 and 5.

In summary, claims 1, 2, 4 and 6 have an effective filing date of 3/27/2003 (the filing date of Application No. 60/458,152), and claims 3, 5, 7, 8, 11-23 and 26-32 have an effective filing date of 9/12/2003 (the filing date of the instant application).

Information Disclosure Statement

Receipt of information disclosure statements, filed on 7/6/2004 and 6/17/2005, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

Figure 2j (Drawings submitted 6/25/2004) contains nucleotide sequences of ten nucleotides each that are not referred to by the use of a sequence identifier. Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

In response to this office action, Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. The nature of the non-compliance did not preclude an examination of the elected invention on the merits, the results of which are presented below.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: panels A and B of

Figure 17 are not separately described. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See paragraph [0094].

The use of the trademarks POLYFECT™ and SUPERFECT™ have been noted in this application at paragraph [0137]. It should be capitalized wherever it appears and be accompanied by the generic terminology. In the instant case, the trademarks are not capitalized.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 1 is objected to because of the following informalities: the numbering of elements and steps is not consistent. The claim lists the features of the polynucleotide construct as elements i-v, and the second and third method steps as steps vi and vii. It would be remedial to amend the claim to remove the reference to "vi" and "vii," because "vi" and "vii" are clearly not part of the construct. The steps may be listed as steps A, B and C. Appropriate correction is required.

Claims 3 and 4 are objected to for the same reasons as applied to claim 1. It would be remedial to amend the claims to replace the reference to "step vi" with a reference to the specific method step (either as step B or by specifically referring to the step of identifying).

Claim 2 is objected to because of the following informalities: the numbering of elements and steps is not consistent. he claim lists the features of the polynucleotide construct as elements i-v, and the second through fourth method steps as steps vi-viii, respectively. It would be remedial to amend the claim to remove the reference to "vi", "vii" and "viii," because "vi", "vii" and "viii" are clearly not part of the construct. The steps may be listed as steps A, B, C and D. Appropriate correction is required.

Claims 5 and 6 are objected to for the same reasons as applied to claim 2. It would be remedial to amend the claims to replace the reference to "step vi" with a reference to the specific method step (either as step B or by specifically referring to the step of identifying).

Claim 21 is objected to because of the following informalities: the last word of the claim should be replaced with the word "vector" to improve the grammar of the claim. Appropriate correction is required.

Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The elected vector, pGT-fs0, does not contain a splice donor, which is required by independent claims 1 and 2 (e.g. specification Table 1 and Figure 2j). Thus, claim 22 is broader in scope than claims 1 and 2.

Claim 23 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 23 depends from claim 8 and requires an additional step to be performed after the amplification of one or more extended cDNA fragments and before the fragments are cloned and sequenced. Claim 8 limits the step of identifying the protein fused to the marker peptide to a SAVI method that consists of the seven steps recited in claim 8. Thus, the inclusion of an additional step to the method of claim 8 is an improper broadening of the claim.

Claim 29 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim 30 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim 31 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and should not depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim 32 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and should not depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7, 8, 13-15, 19-21 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 15, 18-25, 29-35, 76, 77, 79 and 80 of copending Application No. 10/810,976 (hereinafter the '976 application).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 is generic to all that is recited in claims 1-11, 15, 18-25, 29-35, 76, 77, 79 and 80 of the '976 application. That is, claims 1-11, 15, 18-25, 29-35, 76, 77, 79 and 80 of the '976 application fall entirely with the scope of claim 1 of the instant application or, in other words, instant claim 1 is anticipated by claims 1-11, 15, 18-25, 29-35, 76, 77, 79 and 80 of the '976 application. Specifically, the methods of the conflicting claims require the same method steps as the instant claims but further specify the steps of determining the identity of the sequence into which the marker exon has integrated. Instant claims 7 and 8 are anticipated by claims 1, 76, 77 and 79. The conflicting claims set forth the method steps i-vii of claim 8 and 23 (see claim objections), without specifically using the term "inverse polymerase chain reaction." Further, instant claim 13 is anticipated by conflicting claims 9, 23 and 35. Instant claim 14 is anticipated by conflicting claims 7, 8, 21, 22, 33 and 34.

Instant claim 15 is anticipated by conflicting claims 8, 22 and 34. Instant claim 19 is anticipated by conflicting claims 3-6, 15, 18-20 and 29-32. Instant claim 20 is anticipated by conflicting claims 4-6, 18-20 and 30-32. Instant claim 21 is anticipated by conflicting claims 5, 6, 19, 20, 31 and 32.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 7, 8, 11-23 and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "inserted at a random position within two exons" are unclear. It is unclear how a single polynucleotide construct can be inserted within two exons. It is unclear if two separate constructs are randomly integrated into two exons, or if the same construct must integrate into two exons of the same gene. It would be remedial to amend the claim language to clearly indicate that the polynucleotide construct is inserted at a random position between two cellular exons (discussed at page 55, lines 6-7 of the specification).

Claims 3, 4, 7, 8, 11-23 and 26-28 depend from claim 1 and are indefinite for the same reasons as applied to claim 1.

Claim 7 is vague and indefinite in that the metes and bounds of the term Serial Analysis of Viral Integration (SAVI) are unclear. The term is unclear in that it is not explicitly defined in the instant specification and no method steps for SAVI are set forth in the claim. The instant specification describes the SAVI method at paragraph [0044] and Figure 18 G-H. The instant specification incorporates the teachings of US Application No. 09/811,842 by reference. The specification of the 09/811,842 application discloses a SAVI procedure in Figure 17, which differs from the SAVI procedure disclosed in the instant application. Accordingly, the skilled artisan would not be reasonably apprised of the method steps encompasses by the SAVI method when the claim does not set forth any specific positive action method steps to define the SAVI method. It would be remedial to amend the claim language to clearly indicate the method steps encompassed by the SAVI method.

Claim 27 recites the limitation "the oligonucleotide having a specified sequence" in line 2. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to amend the claim to recite the limitation "the oligonucleotide sequence encoding an assayable marker."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 22 is drawn to or encompasses the viral vector pGT-fs0.

The application discloses pGT-fs0, a viral vector that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person

is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description. A statement that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon granting of a patent is also required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 12 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jarvik et al (US Patent No. 5,652,128; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120, 1997; see the entire reference), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

Jarvik et al teach a method of tagging genes and proteins, comprising the steps of (1) randomly introducing a CD-DNA construct by nonhomologous recombination into the genome of eukaryotic cells, (2) identifying those cells that express the CD tagged protein, and (3) determining the sequence identity of the protein or nucleic acid to which the CD tag has been fused (e.g. column 8, line 20 to column 9, line 61; column 4, lines 9-20). Jarvik et al teach that the CD-DNA construct contains a splice acceptor and a splice donor flanking a peptide-encoding segment (e.g. Figure 2). The peptide-encoding segment may encode an epitope that is detected

with an antibody by standard immunological techniques including immunofluorescence, which depends on the interaction of the antibody with the epitope, and immunocytochemical methods (e.g. column 9, lines 42-60). The peptide may be a peptide-encoding sequence that can be read in both directions or in multiple reading frames with the absence of a stop codon (e.g. paragraph bridging columns 8-9). The peptide is fused to an endogenous coding sequence and thus the initiation codon is that of the endogenous coding sequence and not the epitope tag (e.g. column 9, lines 40-60). Jarvik et al teach that the CD-DNA construct is introduced into the eukaryotic cells by a vector such as a plasmid or virus (e.g. column 8, lines 20-38). Jarvik et al do not specify the particular nucleotide sequences present in each segment of the CD-DNA construct and teach that there are many sequences that could serve and that could be used by one skilled in the arts of molecular biology (e.g. column 7, lines 8-12).

Jarvik et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of an oligonucleotide sequence encoding an assayable marker peptide and within the splice acceptor and splice donor sites. Jarvik do not specifically teach the use of retroviruses to deliver the CD-DNA construct.

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope that does not provide the initiation codon and lacks a stop codon, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS)

(e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include a retrovirus comprising the mini-exon cassette taught by Smith as the CD-DNA construct because Jarvik et al teach it is within the ordinary skill in the art to use a virus to deliver a variety of sequences that can be identified and used by one skilled in the art, and Smith suggests the use of the mini-exon for random protein tagging.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a specific sequence to be used in the method, which would be required to actually carry out the method taught by Jarvik, and to provide facile detection of proteins and a faster identification of new genes as taught by Smith. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 12, 14, 15 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jarvik et al (US Patent No. 5,652,128; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120; see the entire reference) further in view of Morin et al (PNAS, Vol. 98, No. 26, pages 15050-15055, 2001; see the entire reference), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

The teachings of Jarvik et al are described above and applied as before.

Jarvik et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of an oligonucleotide sequence encoding an assayable marker peptide and within the splice acceptor and splice donor sites. Jarvik do not specifically teach the use of retroviruses to deliver the CD-DNA construct. Jarvik et al do not teach the splice acceptor and splice donor flanking a green fluorescent protein coding sequence.

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope that does not provide the initiation codon and lacks a stop codon, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS) (e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith

teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

Morin et al teach the inclusion of an enhanced green fluorescent protein (EGFP) coding sequence into an artificial exon used for gene trapping, where the artificial exon contains a splice acceptor His tags, EGFP coding sequence and a splice donor in a 5' to 3' orientation (e.g. Figure 1). Morin et al teach that the inclusion of the EGFP coding sequence into the artificial exon is advantageous when used in gene trapping experiments, because the GFP coding sequence lacks initiation and stop codons and allows the fusion of GFP to the amino- and carboxyl-terminal parts of the trapped protein and allows the GFP coding sequence to be used to determine subcellular localization of the protein (e.g. page 15051, Results).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include a retrovirus comprising the mini-exon cassette taught by Smith as the CD-DNA construct because Jarvik et al teach it is within the ordinary skill in the art to use a virus to deliver a variety of sequences that can be identified and used by one skilled in the art, and Smith suggests the use of the mini-exon for random protein tagging. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the mini-exon cassette of Smith et al to include the EGFP coding sequence of Morin et al, because both Smith et al and Morin et al teach the use of a mini-exon or artificial exon (i.e., a coding sequence flanked by a splice acceptor and splice donor) for gene trapping.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a specific sequence to be used in the method, which would be required to actually carry out the method taught by Jarvik, and to provide facile detection of proteins and a faster identification of new genes as taught by Smith. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. Further, one would have been motivated to include the EGFP coding sequence in order to receive the expected benefit of being able to determine the subcellular localization of the tagged protein.

Claims 1, 12, 14-21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jarvik et al (US Patent No. 5,652,128; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120; see the entire reference) further in view of Morin et al (PNAS, Vol. 98, No. 26, pages 15050-15055, 2001; see the entire reference) and Sinclair (The Scientist, Vol. 15, No. 5, p. 23, 2001; see the entire reference), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

The teachings of Jarvik et al are described above and applied as before.

Jarvik et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of an oligonucleotide sequence encoding an assayable marker peptide and within the splice acceptor and splice donor sites. Jarvik do not specifically teach the use of retroviruses to

deliver the CD-DNA construct. Jarvik et al do not teach the splice acceptor and splice donor flanking a green fluorescent protein (GFP) coding sequence, where the green fluorescent protein coding sequence is a humanized renilla GFP.

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope that does not provide the initiation codon and lacks a stop codon, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS) (e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

Morin et al teach the inclusion of an enhanced green fluorescent protein (EGFP) coding sequence into an artificial exon used for gene trapping, where the artificial exon contains a splice acceptor His tags, EGFP coding sequence and a splice donor in a 5' to 3' orientation (e.g. Figure 1). Morin et al teach that the inclusion of the EGFP coding sequence into the artificial exon is advantageous when used in gene trapping experiments, because the GFP coding sequence lacks initiation and stop codons and allows the fusion of GFP to the amino- and carboxyl-terminal

parts of the trapped protein and allows the GFP coding sequence to be used to determine subcellular localization of the protein (e.g. page 15051, Results).

Sinclair teaches that Stratagene's Vitality™ hrGFP mammalian expression vectors allow protein expression and subcellular localization studies similar to those using jellyfish (*Aquorea victoria*) GFP, except hrGFP is less toxic in many mammalian cells (e.g. page 1/3). Further, Sinclair teaches a construct comprising a FLAG or HA tag followed by an internal ribosomal entry site and an hrGFP coding sequence (e.g. page 2/3). Sinclair teaches that the construct comprising the IRES site allows for detection of the gene of interest by antibodies against FLAG or HA while expression can be monitored by hrGFP detection (e.g. page 2/3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include a retrovirus comprising the mini-exon cassette taught by Smith as the CD-DNA construct because Jarvik et al teach it is within the ordinary skill in the art to use a virus to deliver a variety of sequences that can be identified and used by one skilled in the art, and Smith suggests the use of the mini-exon for random protein tagging. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the mini-exon cassette of Smith et al to include a GFP coding sequence as taught by Morin et al, wherein the GFP coding sequence is hrGFP with or without the IRES sequence, because both Smith et al and Morin et al teach the use of a mini-exon or artificial exon (i.e., a coding sequence flanked by a splice acceptor and splice donor) for gene trapping and Morin et al and Sinclair teach the use of constructs to make GFP fusion proteins.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a specific sequence to be used in the method, which would be required to actually carry out the method taught by Jarvik, and to provide facile detection of proteins and a faster identification of new genes as taught by Smith. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. Further, one would have been motivated to include the hrGFP coding sequence in order to receive the expected benefit of being able to determine the subcellular localization of the tagged protein, as taught by Morn et al, when the IRES site is absent and to determine expression visually when the IRES site is present, as taught by Sinclair. Moreover, one would have been motivated to use the hrGFP coding sequence, because the protein is less toxic than jellyfish GFP in mammalian cells.

Claims 1, 2, 12 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jarvik et al (US Patent No. 5,652,128; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120; see the entire reference) and Keeton et al. Biological Science. 5th Edition. New York: W.W. Norton & Company, Inc., 1993, p. 441), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

The teachings of Jarvik et al are described above and applied as before. Further, Jarvik et al teach the application of the method to the analysis of cellular responses, where CD-tagging is used to identify proteins, and the genes encoding them, whose synthesis is stimulated by a particular treatment, such as the administration of a particular hormone or growth factor to a

particular cell type by comparing treated (i.e., test group) and untreated cells (i.e., reference group) to identify proteins whose levels change in response to the treatment (e.g. column 4, lines 36-46).

Jarvik et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of an oligonucleotide sequence encoding an assayable marker peptide and within the splice acceptor and splice donor sites. Jarvik et al do not specifically teach the use of retroviruses to deliver the CD-DNA construct. Jarvik et al do not specifically teach the use of statistical methods to identify proteins whose levels change among the test and reference groups.

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS) (e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

Keeton et al teach that scientists in all fields of research constantly encounter the same fundamental question—whether deviations that they observe in their experimental results occur by chance or are significant. Keeton et al teach that scientists cannot rely upon a guess and must use a system of standards based upon the mathematical probability that any observed deviation in their sample could have occurred by chance alone. Keeton et al teach that this type of analysis is called statistical analysis (page 441).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include a retrovirus comprising the mini-exon cassette taught by Smith as the CD-DNA construct because Jarvik et al teach it is within the ordinary skill in the art to use a virus to deliver a variety of sequences that can be identified and used by one skilled in the art, and Smith suggests the use of the mini-exon for random protein tagging. Further, it would have been obvious to one of skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include the statistical analysis of the differences between the test and reference groups as taught by Keeton.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a specific sequence to be used in the method, which would be required to actually carry out the method taught by Jarvik, and to provide facile detection of proteins and a faster identification of new genes as taught by Smith. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. One would have been motivated to include statistical analysis of the data in order to

receive the expected benefit of determining whether the result occurred by change or is statistically significant as taught by Keeton et al.

Claims 1, 2-6, 12, 13, 17-21 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jarvik et al (US Patent No. 5,652,128; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120; see the entire reference), Keeton et al. Biological Science. 5th Edition. New York: W.W. Norton & Company, Inc., 1993, p. 441) and Whitney et al (US Patent No. 5,928,888, cited as reference A6 on the IDS filed 7/6/2004; see the entire reference), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

The teachings of Jarvik et al are described above and applied as before. Further, Jarvik et al teach the application of the method to the analysis of cellular responses, where CD-tagging is used to identify proteins, and the genes encoding them, whose synthesis is stimulated by a particular treatment, such as the administration of a particular hormone or growth factor to a particular cell type by comparing treated (i.e., test group) and untreated cells (i.e., reference group) to identify proteins whose levels change in response to the treatment (e.g. column 4, lines 36-46).

Jarvik et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of an oligonucleotide sequence encoding an assayable marker peptide and within the splice acceptor and splice donor sites. Jarvik et al do not specifically teach the use of retroviruses to deliver the CD-DNA construct. Jarvik et al do not specifically teach the use of

statistical methods to identify proteins whose levels change among the test and reference groups. Jarvik et al do not specifically teach the sorting of cells into monoclonal subgroups of genetically identical cells or oligoclonal subgroups of cells based on their differential levels of expression of the marker peptide.

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS) (e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

Keeton et al teach that scientists in all fields of research constantly encounter the same fundamental question—whether deviations that they observe in their experimental results occur by chance or are significant. Keeton et al teach that scientists cannot rely upon a guess and must use a system of standards based upon the mathematical probability that any observed deviation in their sample could have occurred by chance alone. Keeton et al teach that this type of analysis is called statistical analysis (page 441).

Whitney et al teach the tagging of proteins using a construct comprising a splice acceptor and splice donor flanking a nucleic acid encoding a protein with beta-lactamase (BL) activity (e.g. column 12, lines 8-65; Example 1, especially BLEC-3). Whitney et al teach the production of a library of clones, which are separated into two pools by fluorescence activated cell sorting (FACS) using the FRET system: an expressing pool (blue cells) and a non-expressing pool (green cells) to form oligoclonal subgroups based on their differential expression of the marker peptide BL (e.g. paragraph bridging columns 16-17). Further, Whitney et al teach the arrangement of the cells as a panel of single clones (monoclonal) or multiple clones (oligoclonal) (e.g. column 18, lines 41-45). The panels may be used to test compounds by treating the cells and isolating cells by FACS that have up- or down-regulation of gene expression (e.g. paragraph bridging columns 2-3; column 18, line 58 to column 19, line 35). Whitney et al teach that the use of the BL coding sequence is advantageous, because they disclose membrane permeant substrates that allow measurement of BL activity in living cells, which allows functional screening immediately after the rapid identification of a functionally active portion of a genome, without the necessity of transferring the identified portion of the gnome into a secondary screening system (e.g. column 2, lines 16-39).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of protein tagging of Jarvik et al to include a retrovirus comprising the mini-exon cassette taught by Smith as the CD-DNA construct because Jarvik et al teach it is within the ordinary skill in the art to use a virus to deliver a variety of sequences that can be identified and used by one skilled in the art, and Smith suggests the use of the mini-exon for random protein tagging. Further, it would have been obvious to one of skill in the art at the

time the invention was made to modify the method of protein tagging of Jarvik et al to include the statistical analysis of the differences between the test and reference groups as taught by Keeton. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the BL coding sequence taught by Whitney et al into the construct of Smith, because Smith and Whitney teach constructs comprising a splice acceptor and splice donor flanking a reporter sequence. It would have been obvious to one of ordinary skill at the time the invention was made to include the sorting of cells into monoclonal or oligoclonal populations as taught by Whitney et al because Jarvik et al and Whitney et al teach the analysis of the effect of test compounds on tagged cells.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a specific sequence to be used in the method, which would be required to actually carry out the method taught by Jarvik, and to provide facile detection of proteins and a faster identification of new genes as taught by Smith. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. One would have been motivated to include statistical analysis of the data in order to receive the expected benefit of determining whether the result occurred by change or is statistically significant as taught by Keeton et al. One would have been motivated to include the BL coding sequence and sorting of cells as taught by Whitney et al to be able to identify specific cells by using a permeant substrate that allows measurement of BL activity in living cells, which allows functional screening immediately after the rapid identification of a functionally active

portion of a genome, without the necessity of transferring the identified portion of the gnome into a secondary screening system

Claims 1, 11, 12 and 17-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Hopkins et al (WO 00/56874, cited as reference B3 on the IDS filed 7/6/2004; see the entire reference) in view of Smith (BioTechniques, Vol. 23, No. 1, pages 116-120; see the entire reference), as evidenced by the 1996 New England Biolabs, Inc. Catalog, page 39.

Hopkins et al teach a method for determining gene expression comprising the steps of (1) contacting a cell with a recombinant retrovirus containing in a 5' to 3' orientation (i) a branch-point sequence, (ii) a polypyrimidine tract, (iii) a splice acceptor, (iv) a nucleic acid sequence encoding a reporter, (v) a splice donor, and (vi) viral long-terminal repeats, (2) identifying cells that have integrated the cassette and express the reporter polypeptide, and (3) cloning the gene into which the virus integrates by using 5'- or 3'-RACE (e.g. paragraph bridging pages 15-16; page 13; Figure 2B). Hopkins et al teach that the reporter gene can be followed by a stop signal or can be allowed to fuse with the coding sequence of the downstream exon, which may produce a functional protein (e.g. page 10, lines 11-16). Regarding the reporter, Hopkins et al teach that it can be a peptide epitope such as a FLAG, HA or myc epitope, which can be detected by western blot analysis with an antibody that allows detection of enzymatic activity or fluorescence upon interaction of the antibody with the epitope peptide (e.g. paragraph bridging pages 15-16). The initiation codon is provided by the endogenous gene interrupted by the retroviral vector (e.g. page 10, lines 11-16).

Hopkins et al do not teach the sequence of a CD-DNA construct containing (i) a complementary sequence of a first type IIS restriction enzyme recognition sequence and (ii) a second type IIS restriction enzyme recognition sequence, where the sequences are placed on either sited of the nucleic acid sequence encoding an assayable marker peptide (reporter) and within the splice acceptor and splice donor sites

Smith teaches a mini-exon comprising in a 5' to 3' orientation: i) a splice acceptor consensus sequence (3'CS), (ii) the sequence GAGG, a sequence complementary to the MnlI type IIS restriction enzyme recognition sequence, (iii) an oligonucleotide encoding a myc epitope, (iv) the sequence CCTC, a MnlI type IIS restriction enzyme recognition sequence, and (iv) a splice donor (5'CS) (e.g. Figure 1; paragraph bridging pages 117-118). Further, Smith suggests the use of the mini-exon as a tool for gene discovery by placing the mini-exon into introns in a random fashion using retroviruses or bacterial transposons, which would permit the facile detection of proteins. Smith teaches that the mini-exon has the advantage of allowing greater speed of screening for new genes.

The 1996 New England Biolabs, Inc. Catalog (page 39) is cited only to show that the recognition sequence for MnlI is 5'-CCTCNNNNNNN-3'.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Hopkins et al to include the mini-exon taught by Smith either with or without the addition of a stop codon to the end of the myc epitope because Hopkins et al teach it is within the ordinary skill in the art to use a vector construct comprising each of the features disclosed by Smith et al but do not provide a specific sequence and Smith et

al teach the sequence of a mini-exon that includes the splice acceptor, reporter and splice donor sequences taught by Hopkins et al.

One would have been motivated to make such a modification in order to receive the expected benefit of using the mini-exon of Smith et al to identify the random insertions of the retroviral vector in a facile manner with a greater speed of screening as taught by Smith et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

CELINE QIAN, PH.D.
PRIMARY EXAMINER

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.